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Acampomelic Campomelic Dysplasia: Further Radiographic Variations

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Acampomelic campomelic dysplasia (ACD) is a rare genetic syndrome affecting bone and connective tissue. This syndrome is a variant of the more commonly encountered campomelic dysplasia but is characterized by the absence of long bone curvature (acampomelia). Affected children have a characteristically flat facial profile and present with respiratory distress. They all have markedly hypoplastic scapulae. We present two sisters with ACD between whom there were some clinical and radiographic differences and also variations from the classic CD. We describe shallow orbits, a radiographic finding that has not been previously documented in this dysplasia. Am. J. Med. Genet. 69:29–32, 1997. © 1997 Wiley-Liss, Inc.

KEY WORDS: campomelic dysplasia; acampomelic variant; hypoplastic scapulae; respiratory distress; tracheal abnormality; shallow orbits

INTRODUCTION

Acampomelic campomelic dysplasia (ACD) has been described in a number of case reports [Lindgren and Ringertz, 1980; Macpherson et al., 1989; Friedrich et al., 1992]. Abnormalities in this syndrome are encountered in the skeleton and respiratory tract. We present two female siblings with clinical and radiologic findings diagnostic of campomelic dysplasia (CD) but without bowing of the long bones. There were radiographic differences between the two. We wish to emphasize these radiographic variations between the two children and compare with the classical and better known form of CD with

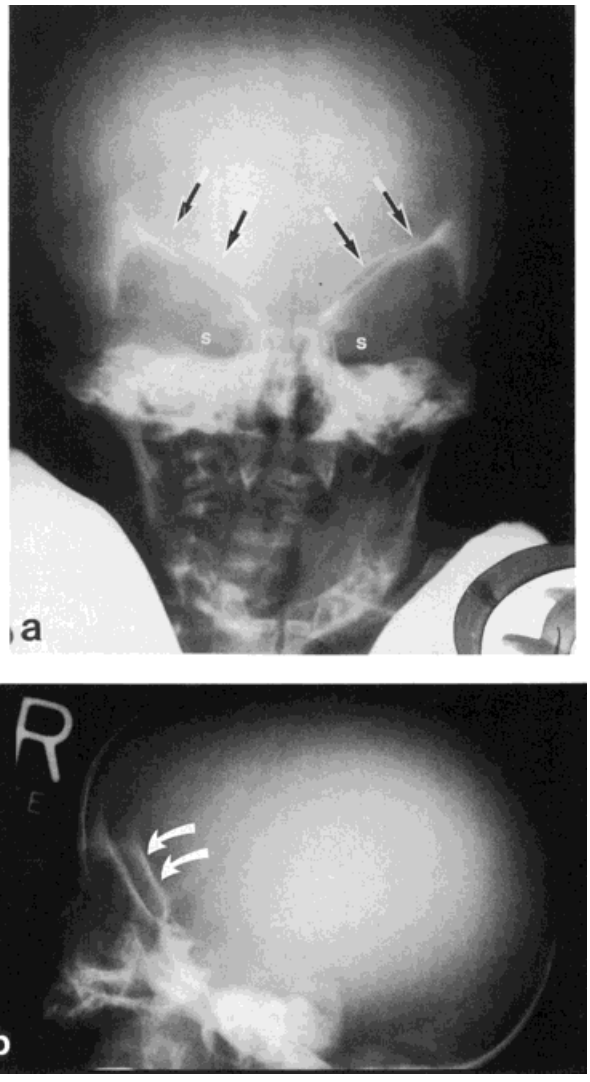

Fig. 1. Patient 1, newborn. Frontal (**a**) and lateral (**b**) skull radiographs demonstrate shallow orbits with angulation of the orbital roofs (arrows) and vertical posterior orbital walls (curved arrows). The superior orbital fissures(s) are large.

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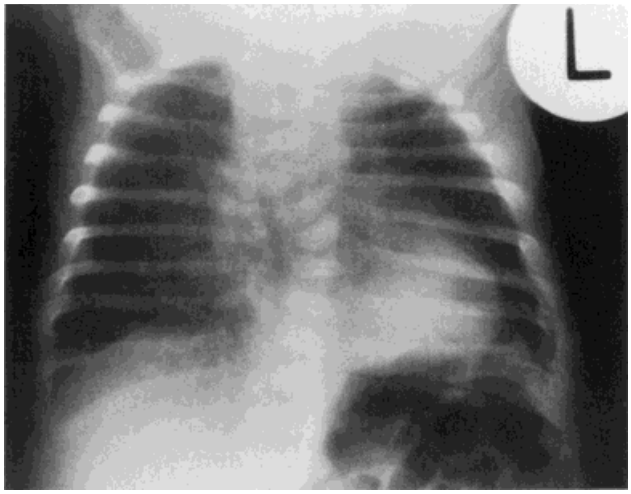

Fig. 2. Patient 1, newborn. Frontal chest radiograph with 11 pairs of ribs. Irregularly shaped vertebrae are present with a thoracic levoscoliosis. Scapulae are hypoplastic.

bowing of long bones. We describe radiographic findings in the orbits not previously reported in this dysplasia.

CLINICAL REPORTS

Two girls with ACD were born to nonconsanguineous parents. The maternal obstetric history was complicated by one spontaneous abortion. The parents had two other healthy daughters. The pregnancies were uncomplicated, and both girls were delivered via elective cesarean section at 39 weeks gestation because of a maternal bifid uterus. Prenatal sonography showed no evidence of long bone bowing at 16 weeks.

The children were of appropriate size for gestational age. Their facial profiles were flat with biparietal prominence and flat forehead. Interpupillary distances were at the 50th percentile. Palpebral fissures were neutral in Patient 1 and downslanting in Patient 2; both had minimal epicanthal folds bilaterally. The eyes were proptotic, and the nasal bridge was flat. Their ears were low-set and dysplastic, and both children had severe conductive hearing loss. The palate was intact in Patient 1, and a small posterior palatal cleft was present in Patient 2. In both children the neck was short and the trunk also, causing the chest to appear wide. Pectus excavatum was present in both. The nipples of the two children were hypoplastic. The extremities were shortened in the mesomelic segments. The fingers were tapered distally, and clinodactyly of digit 5 was present. Muscle tone was decreased in Patient 1 but normal in Patient 2. External female genitalia were normal. Both had normal chromosomes (46, XX).

The two children exhibited poor growth and weight gain, and both were severely developmentally delayed. They experienced numerous episodes of respiratory distress and pneumonia, including aspiration pneumonia. Patient 2 required a tracheostomy to relieve her breathing difficulty; bronchoscopy at 2.5 years showed abnormal laryngeal position and bronchomalacia. The older child died of respiratory complications at age 4; the second child is still alive at age 5.

Radiographic Findings

The radiographic bone density was normal. The skull was scaphocephalic in Patient 1 and normal in shape in Patient 2. In both children, the orbits were shallow, with almost vertical orientation of the posterior portion of the orbital roofs on the lateral projection and abnormally angulated roofs on the frontal projection (Fig. 1a,b). The superior orbital fissures were enlarged (Fig. 1a).

Both children had hypoplastic cervical vertebrae. Thoracic scoliosis was present from birth in Patient 1, and abnormally shaped vertebrae were present at the apex of the thoracic curve (Fig. 2). Patient 2 had incomplete fusion of the posterior thoracic neural arches and platyspondyly, and she developed kyphoscoliosis in

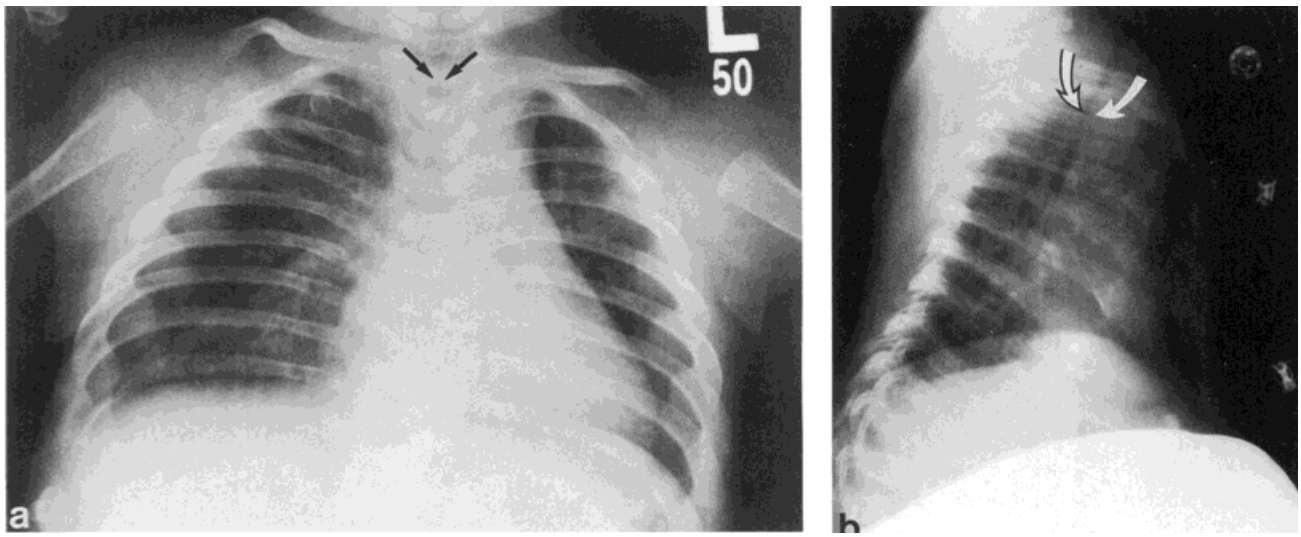

Fig. 3. Patient 2, at 4 months. Frontal (left) and lateral (right) chest radiographs. The vertebrae are flattened, the pedicles are not visualized, and the posterior neural arches are unfused (arrows). The sternum is unossified. Scapulae are hypoplastic. The intrathoracic airway is narrowed (curved arrows).

the second year of life. The pedicles were not ossified in the mid-thoracic spine. The ribs were thin; 11 pairs of ribs were present in Patient 1, and 12 pairs were present in Patient 2. The sternum was incompletely ossified in both. The scapulae were hypoplastic (Figs. 2, 3a). Airway narrowing was best visualized radiographically on the lateral projection (Fig. 3b).

Long bones were normal in shape, without bowing (Fig. 4). The lower limbs were shortened in the mesomelic portion. Femoral and tibial ossification centers were not visualized. The iliac bones and ischia were vertical in orientation (Fig. 5). The pubis was poorly ossified in both, although this was more marked in Patient 2.

DISCUSSION

CD [Houston et al., 1983] is a common skeletal disorder, caused in many cases by heterozygosity for mutations in the SOX9 gene [Wagner et al., 1994]. Consistent with this, Lynch et al. [1993] suggested that inheritance may be autosomal dominant in some families. Several studies have shown 46,XY karyotypes in phenotypic females [Maraia et al., 1991]. CD includes two presentations: the more common short-limbed type that may be either normocephalic or with craniosynostosis, and a rarer long-limbed type [Khajavi et al., 1976].

There have been reports of patients with the findings of CD, but whose long bones were not bowed, i.e., acampomelic campomelia [Macpherson et al., 1989; Ninomiya et al., 1995]. A single patient described by Friedrich et al. [1992] had mildly bowed tibiae.

ACD is a variation of CD and manifests wide radiographic variability even within the same family, as demonstrated by the two siblings described in this report. Radiographic variation between the two was encountered in the skull, ribs, vertebrae, and pubis. Hall and Spranger [1980] have proposed major diagnostic criteria for CD, including lower extremity bowing, absent or hypoplastic scapulae, nonmineralized thoracic pedicles, and narrow vertical iliac bones; among the minor criteria are wide spacing of ischial bones as well as absence of distal femoral and proximal tibial epiphyses. Hypoplasia of the scapulae is generally considered one of the most important and unique radiographic features in patients with ACD and CD. The authors are aware of only a single report of a child with major criteria of CD in whom the scapulae were normal [Austin et al., 1980].

The orbits were shallow in both siblings. The posterior orbital walls were vertical in orientation, the orbital roofs were angulated, and the orbital fissures were widened. This appearance was symmetric and present in both children. Shallowness of the orbits manifests clinically as proptosis. To the best of our knowledge, these radiographic findings in the orbits have not been previously documented in ACD.

Both children had significant airway compromise from birth. The cartilage abnormalities in CD result from structurally abnormal tracheobronchial cartilages that are reduced in number in the larger airways and totally absent in the smaller bronchi. These abnormalities weaken the airways and cause them to collapse in both phases of respiration [Grad et al., 1987]. Elective tracheostomy will maintain patency of the large airways, relieve breathing difficulty, and prolong survival. However, respiratory tract infection remains a potentially life-threatening problem.

The etiology of the developmental delay is uncertain. Severe mental retardation may be a pleiotropic effect of the syndrome or may be due to severe anoxia. The associated hearing loss contributes to learning difficulty.

The diagnosis of ACD is difficult and depends on a combination of clinical and radiographic findings. The chest radiograph is most commonly the initial diagnostic procedure to evaluate respiratory distress, and this

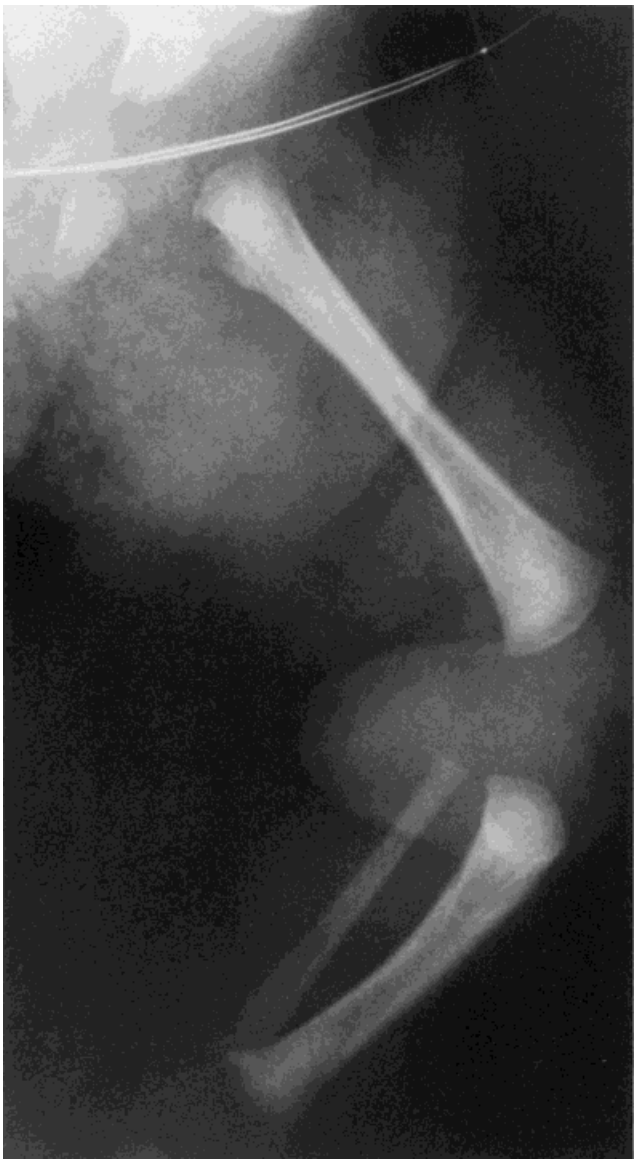

Fig. 4. Patient 2, newborn. Lateral radiograph of the left lower limb without bowing of the long bones.

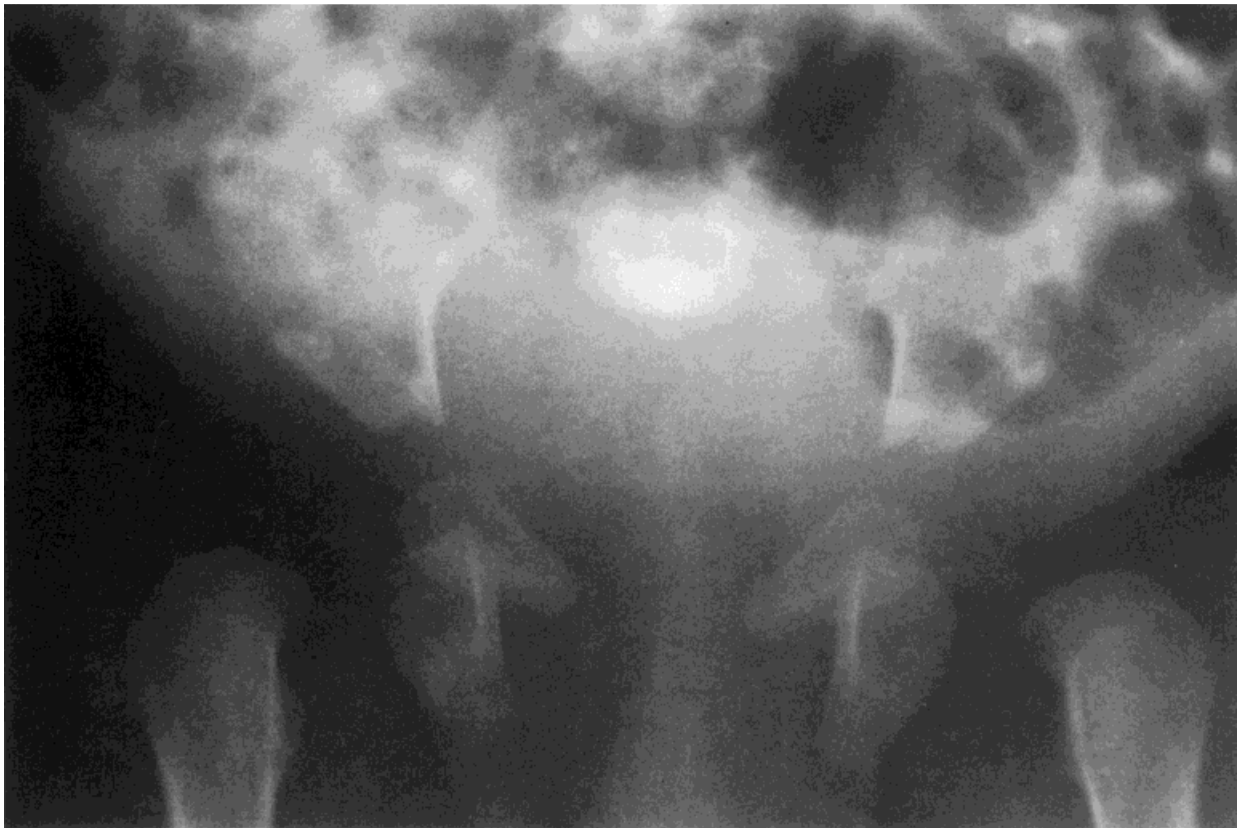

Fig. 5. Patient 2, newborn. Radiograph of the pelvis with vertical orientation of the ilia and ischia. The pubis is hypoplastic.

facilitates early diagnosis because many features of ACD are present on the radiograph. It is likely that the abnormalities on the chest radiograph will indicate need for a skeletal survey, and it is important that the acampomelic appearance of the lower limb bones does not mislead the clinician from the diagnosis of this variant of CD. We stress that the diagnosis of ACD should be considered in a neonate with respiratory distress and minor or major anomalies. It is important that the correct diagnosis may not be considered because of a normal prenatal sonogram demonstrating straight limbs or acampomelia. Early diagnosis enables timely treatment for the jeopardized airway, with elective tracheostomy to relieve the severe tracheomalacia if full resuscitative efforts are considered appropriate.

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